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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
LI, QIAN J

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/823,699	Applicant(s) KANO ET AL.	
	Examiner Janice Li	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

DETAILED ACTION

Claims 1-11 are pending in the application and under current examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention (see *In re Wands*, 858 F. 2d 731, 737, 8 USPQ 2d 1400, 1404, 1988). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the breadth of the claims, and amount of direction provided.

Claim 1 recites "a vaccine", claim 5 recites "a method for vaccination". The specification defines "the term "vaccine" used herein means a composition used for prevention or treatment of an infectious disease" (page 10, line 3). These claims clearly state the intended use of the composition and the method. With respect to claim

breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. "WHEN A COMPOUND OR COMPOSITION CLAIM IS LIMITED BY A PARTICULAR USE, ENABLEMENT OF THAT CLAIM SHOULD BE EVALUATED BASED ON THAT USE". (MPEP 2164.01c) When analyzing the enabled scope of the claims, the intended use is to be taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification. "A vaccine composition", or "a method for vaccine" are defined as a composition and method for therapeutic use, to prevent, alleviate, treat, or cure a disease within the animal to which the substance is administered, therefore, will be evaluated by the standard. Claims 9 and 10 are drawn to inoculating a DNA vaccine prior to inoculating a Sendai virus vaccine for immunodeficiency virus, the recited DNA vaccine embraces *any* DNA vaccine, i.e. using any DNA viral vector for any pathogens. As such, the broadest reasonable interpretation of the claimed invention properly encompasses genetic vaccination for immunodeficiency virus for any animal including human using Sendai virus vaccine for SHIV and in combination with any DNA vaccines; therefore, the claims will be evaluated by that standard.

In view of the guidance provided, the specification teaches the construction of Sendai virus vectors encoding SIV-Gag protein, and using such to induce an antigen-specific cellular immune response *in vitro*, and in vivo by intranasal administration in cynomolgus macaques. In the *in vivo* experiments, SIV-Gag expression was detected in the nasal mucosa and local lymphnodes of the nasal cavity, the infected cells could stimulate a Gag-specific CD8+ T cells in vitro, and the frequencies of Gag-specific

CD8+ T cells in PBMC was higher compared to control groups, but Gag-specific antibody is undetectable in the plasma. In another experiment (example 9), SeV-SIV-Gag was combined with a DNA vaccine for administration. Upon a subsequent challenge with SHIV, the vaccinated rhesus macaques show changes in cell counts of peripheral blood CD4+ and lower copy numbers of SHIV RNA in the plasma. However, the specification fails to teach whether prior administration of *any* DNA vaccine would function synergistically with the SeV-SIV-Gag, whether the SeV-SIV-Gag induced changes in CD8+ cells is sufficient to elicit a protective response against SHIV, whether SeV-SIV-Gag alone could achieve any protective effect against SHIV infection either in monkeys or in humans, and whether the protective effect obtained in the DNA-RNA combination regimen is attributed, solely or predominantly, to the DNA vaccine. The specification fails to provide sufficient guidance for the skilled artisan to practice the invention without undue experimentation.

In view of the state of the art in developing vaccine for AIDS, many reports have indicated certain degree of success in inducing a specific humoral and cellular immune response and in providing certain degree of protection against SHIV using DNA virus vectors (*Seth et al* (Proc Natl Acad Sci USA 1998;95:10112-6) or *Flanagan et al* (J Gen Virol 1997;78:991-7). *Ourmanov et al* (J. Virol. 2000;74:2740-2751, IDS) teach "AIDS VACCINES THAT ARE BASED ON RECOMBINANT VIRAL VECTORS SUCH AS POXVIRUSES, ALPHAVIRUSES, AND ADENOVIRUSES APPEAR TO PROVIDE SOME PROTECTION IN PRIMATE MODELS...STUDIES WITH MACAQUES IMMUNIZED WITH RECOMBINANT VACCINES BASED ON NYVAC HAVE DEMONSTRATED PARTIAL PROTECTION ... AND CURRENTLY BEING EVALUATED IN CLINICAL TRIALS IN HUMANS" (introduction), however, "the level of protection from AIDS was clearly less than

optimal". The above teachings indicate that at the time of instant filing, AIDS vaccine is still underdevelopment, the results of using such in humans are unpredictable, hence resulting in a trial and error situation.

In view of the state of the art in vaccination for human, *McCluskie et al* (Mol Med 1999 May;5:287-300) TEACH "UNFORTUNATELY, THE PROMISING RESULTS IN ANIMAL MODELS HAVE NOT BEEN REALIZED IN HUMAN TRIALS AND CONSIDERABLE EFFORT IS NOW BEING FOCUSED AT UNDERSTANDING THIS DIFFERENCE AND DEVELOPING WAYS OF IMPROVING THE EFFICACY OF DNA VACCINES." (See 1st paragraph of the introduction) "HOWEVER, THE RESULTS IN MICE WERE NOT ALWAYS PREDICTIVE OF THOSE IN MONKEYS AND THIS IS LIKELY TRUE FOR HUMANS AS WELL. OPTIMAL DOSE AND IMMUNIZATION SCHEDULE WILL MOST LIKELY VARY BETWEEN SPECIES. IT IS NOT CLEAR WHETHER RESULTS IN NON-HUMAN PRIMATES WILL BE PREDICTIVE OF RESULTS IN HUMANS, THUS ADDITIONAL STUDIES ARE REQUIRED." (See abstract) The instant specification does not provide any *in vivo* data showing that the instant invention has overcome the deficiency present in the prior and post-filling art. Thus, it would require undue experimentation for any person skilled in the art to practice the instant invention with SeV-SIV-Gag alone or in combination with a DNA vaccine in humans.

From the discussion above, it is evident that at the time of the invention, the gene therapy practitioner, while acknowledging the significant potential of genetic vaccination, still recognized that such therapy was neither routine nor accepted, and awaited significant development and guidance for its practice. Therefore, it is incumbent upon applicants to provide sufficient and enabling teachings within the specification for such therapeutic regimen. Although the instant specification provides some *in vitro* and *in vivo* data indicating a potential therapeutic use of the claimed vectors, it is not enabled

for its full scope because the specification does not disclose any protective effect using SeV-SIV-Gag alone *in vivo* or the DNA-RNA combination in humans. In summary, the teachings and guidance present in the specification, as a whole, represent an initial investigation into the feasibility of the development of a useful means for developing HIV vaccine which awaits further development to the practical level.

Accordingly, in view of the quantity of experimentation necessary to determine the parameters for achieving vaccine effect for immunodeficiency virus, the lack of direction provided by the specification as well as the absence of working examples with regard to *in vivo* protective effect using SIV-SeV alone or in combination with DNA in humans, it would have required undue experimentation for one skilled in the art to make and/or use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 10 are vague and indefinite because they recite, "inoculating a DNA vaccine". It is unclear whether the DNA vaccine is immunodeficiency virus-specific or any DNA vaccine, thus, the metes and bounds of the claims are unclear.

Claim 11 is vague and indefinite because it is incomplete. The claim calls for inducing a specific cellular immune response to immunodeficiency virus, however there

is no positive step recited that clearly relates back to the preamble. Further, the claim as written embraces both an *in vitro* and *in vivo* method, however, it is unclear how to introducing the vector specifically to APCs *in vivo*, and how to contact the APC with the particular recited T cell groups, thus, the metes and bounds of the claim are unclear. Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter that claims encompass as well as make clear the subject matter from which others would be precluded, *Ex parte Erlich*, 3 USPQ2d 1011 at 6.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by *Yu et al* (Genes Cells. 1997 Jul;2:457-66).

These claims are drawn to a composition comprising a Sendai virus vector encoding a viral protein of an immunodeficiency virus, wherein the Sendai virus vector is defective in V gene.

Yu et al teach a Sendai virus vector defective in V gene encoding a virus protein (gp120) of the human immunodeficiency virus (abstract). Thus, *Yu et al* anticipate instant claims.

Please note that the claim recitation "a vaccine" has not been given patentable weight in the instant rejection because the intended use for immunogenicity does little toward defining structure of the claimed invention. Rather, polynucleotide sequences, vector components are relied upon for structural determination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Yu et al* (Genes Cells. 1997 Jul;2:457-66) as applied to claims 1 and 3 above, and further in view of *Flanagan et al* (J Gen Virol 1997;78:991-7).

These claims are drawn to a composition comprising a Sendai virus vector encoding a viral protein of an immunodeficiency virus, preferably the viral protein is a Gag protein, wherein the Sendai virus vector is defective in V gene.

Yu et al teach a Sendai virus vector defective in V gene encoding a virus protein of the human immunodeficiency virus, and go on to teach that the deletion of the nonessential V gene leads to greater expression of a viral protein (abstract). *Yu et al* do not teach a Gag protein. *Flanagan et al* teach a vector encoding SIV Gag protein.

Flanagan et al go on to teach that although both the Env and Gag could serve as an antigen for HIV vaccine, the variability of the *env* gene makes the Env protein a difficult antigen for a vaccine to target, whereas more conserved Gag protein is a potent stimulator of both the cellular and humoral components of the immune system and may contain important protective epitopes (2nd paragraph on left column in page 992).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the vector taught by *Yu et al*, by simply substitute the env gene (gp120) with that of the Gag as taught by *Flanagan et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the vector for efficient production of Gag protein. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Please note that the claim recitation "a vaccine" has not been given patentable weight in the instant rejection because the intended use for immunogenicity does little toward defining structure of the claimed invention. Rather, polynucleotide sequences, vector components are relied upon for structural determination.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Steinman et al* (US 6,300,090), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66) and *Seth et al* (Proc Natl Acad Sci USA 1998;95:10112-6).

This claim is drawn to a method for inducing cellular immune response to a viral protein of an immunodeficiency virus comprising (a) introducing a Sendai virus vector encoding said viral protein into an antigen presenting cell, (b) contacting the APC with a T helper cell and a cytotoxic T cell.

Steinman et al teach a method comprising providing antigens to dendritic cell (APC) using a viral vector including Sendai virus; which vector may be modified to express non-native antigens for presentation to the DCs, the transfected DCs are then capable of presenting the antigen to T cells inducing cytotoxic T lymphocyte activity (abstract and column 18, line 40). *Steinman et al* do not particularly teach a Sendai virus encoding HIV derived protein.

Yu et al teach a Sendai virus vector encoding a virus protein (gp120) of the human immunodeficiency virus. *Yu et al* also teach that the vector system could be used for broad applications including vaccine development (right column in page 457).

Seth et al teach, " WITH ACCUMULATING EVIDENCE THAT VIRUS-SPECIFIC CYTOTOXIC T LYMPHOCYTES (CTLS) ARE IMPORTANT IN CONTAINING THE SPREAD OF HIV-1 IN INFECTED INDIVIDUALS, A CONSENSUS HAS EMERGED THAT AN HIV-1 VACCINE SHOULD STIMULATE THE GENERATION OF CTLS". (1st paragraph, page 10112)

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Steinman et al*, by simply employ the vector taught by *Yu et al* in the process taught by *Steinman et al* with a reasonable expectation of success in inducing a specific cellular immune response. The ordinary skilled artisan would have been motivated to modify the method because it could better stimulate HIV or SIV specific CTLs. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
May 6, 2002

JAMES KETTER
PRIMARY EXAMINER